REMARKS

The Claim Amendments

Applicant has cancelled non-elected claims 8-20.

Applicant has amended the claims, as suggested by the Examiner and as described further below.

Applicant has amended claim 5 to recite a vector comprising a DNA molecule of claim 1 or 2. Support for this amendment can be found throughout the specification, e.g., at page 7, first full paragraph.

Applicant has amended claim 6 to recite a prokaryotic or eukaryotic host cell stably transformed or transfected by a vector comprising a DNA molecule of claim 1 or 2. Support for this amendment can be found throughout the specification, e.g., at page 7, second full paragraph.

Applicant has amended claim 7 to recite that the host cell transformed or transfected with a DNA molecule of any one of claims 1-4. Support for this amendment can be found throughout the specification, e.g., at page 5, second full paragraph and pages 6-7.

Applicant makes these amendments expressly without waiver of his right to file for and to obtain claims directed to the cancelled or amended subject matter in this application or in divisional or continuing applications claiming priority and benefit herefrom.

Upon entry of the above amendments, claims 1-7 are now pending in this application. None of the amendments to the claims constitutes new matter.

The Office Action

35 U.S.C. §101 – Non-Statutory Subject Matter

Claim 2 stands rejected under 35 U.S.C. § 101, as purportedly being directed to non-statutory subject matter. The Examiner states that the claimed DNA is a product of nature and is not patentable because the claim does not indicate that the DNA is isolated.

Applicant has obviated the rejection by amending claim 2 to recite "an isolated DNA molecule", as suggested by the Examiner.

35 U.S.C. § 101 – Utility and 35 U.S.C. § 112, first paragraph – Enablement

Claims 1-7 stand rejected under 35 U.S.C. § 101 as purportedly being unsupported by a substantial or well established utility and thus purportedly lacking enablement under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner states that the claims are drawn to a DNA molecule comprising a sequence that is at least 80% homologous to SEQ ID NO: 1-3, as well as a vector comprising the DNA molecule, a host cell comprising the vector and a process for making the polypeptide encoded by the DNA using the host cell. According to the Examiner, claim 3 encompasses sequences which encode polypeptides that do not have any particular function and can include non-functional variants or variants with a different function from the polypeptides encoded by SEQ ID NOS: 1-3, because the claim encompasses variants that are at least 80% homologous to SEQ ID NOS:1-3 and does not specifically indicate that the encoded

polypeptide has any particular function. Applicant traverses, in view of the claim amendments and the following remarks.

Applicant has amended claim 3 to recite a purified and isolated DNA molecule comprising a DNA sequence which is at least 95% homologous to a DNA sequence selected from the group consisting of SEQ ID NO 4, SEQ ID NO 5 and SEQ ID NO 6 and which encodes a polypeptide with the immunological activity of BMOG. Support for this amendment can be found, e.g., on page 11, last paragraph and page 20, third paragraph (providing literal support for sequences that are most preferably 95% homologous to the polypeptide of SEQ ID NOS: 4-6); page 6, second full paragraph and page 9, last paragraph (teaching a regulatory role for BMOG in immunological function).

Applicant has also amended claim 4 to recite the DNA molecule of claim 2, further characterized by encoding a polypeptide with the immunological activity of BMOG, wherein one or more amino acids of said amino acid sequence are substituted, deleted or inserted. Support for this amendment can be found, e.g., at page 20, first full paragraph; and page 13, last paragraph (teaching preferred biologically active fragments of BMOG with one or more amino acid substitutions, deletions or insertions); page 6, second full paragraph and page 9, last paragraph (teaching a role for BMOG in immunological function); pages 2-3, first paragraph of the Summary; and page 3, first full paragraph (teaching that variant forms of the BMOG polypeptide can activate or block immunological events).

The present invention is directed to DNA and amino acid sequences of C-terminal splicing variants of human BMOG, including DNA sequences encoding human

BMOG which may assume three different forms of BMOG depending on the splicing point of the last exon (see, page 3, lines 5-6). The specification as filed discloses several credible specific and substantial utilities for the claimed sequences. The specification describes how BMOG polypeptides could be formed to: (1) activate or block immunoregulatory events, by coupling to other proteins, such as an immunoglobulin Fc domain, to confer favorable properties, such as a long serum half-life or (2) block interaction between cell surface BMOG and a receptor protein (i.e., to identify a novel BMOG receptor; see, pages 2-3; and page 11).

The specification also discloses that BMOG polypeptides are useful as diagnostic markers for BMOG in disease states. The proteins can be used to raise BMOG-specific antibodies and these anti-BMOG antibodies are also a component of this invention. These antibodies may either block immunological responses or may be incorporated into diagnostic tests (see, page 3, second full paragraph).

The specification also discloses experimental evidence establishing that BMOG transcripts are relatively limited to germinal center B cells, indicating a role for BMOG in immunological function (see, page 6, second full paragraph). The immunomodulatory role of BMOG has also been confirmed by BMOG's identification as a receptor on natural killer (NK) cells that induces the cells to become cytotoxic. For example, Pende et al. ("Identification and molecular characterization of NKp30, a novel triggering receptor involved in natural cytotoxicity mediated by human natural killer cells," J. Exp. Med., 190, 1505–1516, 1999; hereinafter "Pende et al.") (attached hereto as Exhibit A), identified a receptor polypeptide termed NKp30, which is expressed by all resting and

activated human NK cells. Using monoclonal antibodies that recognized NKp30, Pende et al. showed that crosslinking of NKp30 induced strong NK cell activation, as demonstrated by their increased cytolytic properties. See, Pende et al., page 1509, right column and page 1510, Figure 4A. Pende et al. also showed that by masking the anti-NKp30 antibodies, and thus preventing crosslinking of NKp30, NKp30 lacked the ability to stimulate NK cells to kill a target cell. Further, Pende et al. characterize NKp30 at the nucleotide and amino acid level and thus illustrate that it is a receptor molecule that is identical to the BMOG receptor polypeptide of SEQ ID NO. 4 of the present application. Thus, BMOG has been confirmed to be an immunoregulatory agent involved in natural cytotoxicity.

In an independent study, Ferlazzo et al. ("Human dendritic cells activate resting natural killer (NK) cells and are recognized via the NKp30 receptor by activated NK cells," J. Exp. Med., 195, 343–351, 2002; hereinafter "Ferlazzo et al."), (attached hereto as Exhibit B), showed that NK cells are activated by both mature and immature dendritic cells and that such activation of NKp30, i.e., BMOG. As part of the immune response, dendritic cells (DCs) exist in immature form and take up substrates, such as proteins and dying cells, from the cellular environment. When stimulated by inflammatory cytokines or microbial antigens, DC cells undergo maturation and mobilize resting human NK cells. Ferlazzo et al. show that NKp30 is the primary activating signal of NK cells, which can kill immature DCs. See, Ferlazzo et al., page 347, left column and Figure 5. Thus, BMOG is directly involved as an intracellular mediator in the generation of an immune response.

NK cells are important members of the immune response and are involved in the control of tumor growth, viral and microbial defense, autoimmunity and transplant rejection. Moretta et al. ("What is a natural killer cell?", Nature Immunol., 3, 6–8, 2002; hereinafter "Moretta et al."), (attached hereto as Exhibit C), describes the possibility of exploiting NK cells in therapy, such as in the fields of infectious diseases, cancer and bone marrow transplantation. See, Moretta et al., page 8. NK cell alloreactivity was shown in acute myeloid leukemia patents that were undergoing allogenic bone marrow grafting, leading Moretta et al. to postulate that "NK cell alloreactivity in response to mismatches for MHC class 1 alleles may greatly favor the occurrence of graft–versus–leukemia in the absence of graft–versus–host responses" and suggest that "NK cell-based adoptive immunotherapy may become a potent tool with which to prevent leukemic relapses, not only after bone marrow transplantation but also after chemotherapy." See, Moretta et al., page 8.

These documents confirm applicant's teaching of DNA molecules encoding BMOG polypeptides as new MOG family members that those of ordinary skill in the art would appreciate to be useful as diagnostic markers for and in the treatment of immune-based disease. To meet the utility requirement of 35 U.S.C. §§ 101 and 112, first paragraph, a patent application must describe an asserted utility with specificity, but it need not demonstrate utility to a certainty. In Carl Zeiss Stiftung v. Renishaw PLC, 945 F.2d 1172, 1180 (Fed. Cir. 1991). If a claimed invention meets at least one stated objective, utility under § 101 is clearly shown. Raytheon Co. v. Roper Corp., 724 F.2d 951,958 (Fed. Cir. 1983). Proof of one of the disclosed utilities suffices to meet the

statutory utility requirement. See Standard Oil Co. v. Montedison, S.p.a., 664 F.2d 356, 375 (3d Cir. 1981). The well-documented involvement of BMOG in the immune response confirms that the instant invention has a stated, specific and credible utility. Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1-7 under 35 U.S.C. §§ 101 and 112, first paragraph.

35 U.S.C. §112, First Paragraph – Written Description

Claims 3-4 stand rejected under 35 U.S.C. § 112, first paragraph, as purportedly lacking written description. The Examiner contends that claims 3 and 4 are drawn to a genus of polypeptides that are defined only by sequence homology, because claim 3 does not required that the encoded polypeptide possess any particular biological activity and neither claim requires that the sequence possess any particular conserved structure or other distinguishing feature. The Examiner states that in the absence of sufficient recitation of distinguishing identifying characteristics, such as a recitation of a particular portion of the structure that must be conserved between the variant sequences or an indication of which sequences are critical for the encoded peptide to have the biological activity of BMOG, there is no adequate written description of the claimed genus. Applicant traverses, in view of the foregoing claim amendments and the following remarks.

Applicant has amended claims 3 and 4 to recite DNA sequences that are defined both by sequence homology (claim 3) or sequence substitution, deletion or insertion (claim 4) and biological activity. Every member of the genus of claimed DNA

molecules encodes a polypeptide with both (a) a common structural feature, i.e., sequences that are at least 95% homologous to the amino acid sequence of SEQ ID NOS: 4-6, or have at least one substitution, deletion or insertion from the amino acid sequence of SEQ ID NOS: 4-6, and (b) a common function that corresponds to the common structural feature and is shared by all members of the claimed genus, i.e., the biological or immunological activity of BMOG.

Thus, the instant application teaches a structure/function relationship for the shared structural feature of the claimed DNA molecules. With these claim amendments, therefore, the written description requirement has been satisfied. Accordingly, applicant requests that the Examiner reconsider and withdraw this rejection.

CONCLUSION

Applicant requests favorable consideration and early allowance of the pending claims. Applicant invites the Examiner to telephone the undersigned if a telephonic discussion would facilitate resolution of any outstanding issues in the case.

Respectfully submitted,

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